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Attorney Docket No. 9233-54

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Ekwuribe et al.
Serial No.: 09/873,899
Filed: June 4, 2001

Confirmation No.: 5139
Group Art Unit: 1615

#11

For: *MIXTURES OF INSULIN DRUG-OLIGOMER CONJUGATES COMPRISING
POLYALKYLENE GLYCOL, USES THEREOF, AND METHODS OF MAKING
SAME*

Date: January 10, 2003

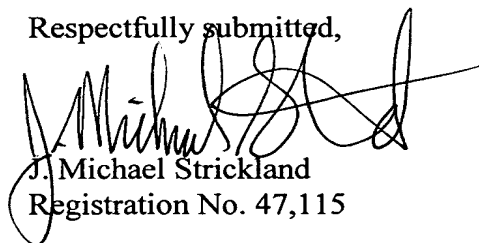
Commissioner for Patents
Washington, DC 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

Attached is a form PTO-1449, together with a copy of the identified document(s). This Information Disclosure Statement is submitted in accordance with 37 C.F.R. § 1.97(b), within three months of the filing date of the above-referenced application or before the mailing of a first Office Action on the merits, whichever event occurs last. Accordingly, no fee is required. The Commissioner is authorized to charge any additional fee, or credit any refund, to our Deposit Account No. 50-0220.

Respectfully submitted,


J. Michael Strickland
Registration No. 47,115

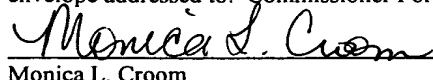


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FORM PTO-1449 U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket Number
9233-54

Serial No.
09/873,899

LIST OF DOCUMENTS CITED BY APPLICANT

(Use several sheets if necessary)

Applicants: Ekwuribe et al.

Filing Date: 06/04/01

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U. S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
JRL	1.	3,919,411	11/11/75	Glass et al.	424	78.27	
JRL	2.	3,256,153	06/14/66	Heimlech	424	497	
JRL	3.	3,868,356	02/25/75	Smyth	530	303	
JRL	4.	3,950,517	04/13/76	Lindsay et al.	514	3	
JRL	5.	4,003,792	01/18/77	Mill et al.	530	303	
JRL	6.	4,044,196	08/23/77	Huper et al.	526	271	
JRL	7.	4,087,390	05/02/78	Shields	525	54.11	
JRL	8.	4,093,574	06/06/78	Shields	525	54.11	
JRL	9.	4,100,117	07/11/78	Shields	525	54.11	
JRL	10.	4,229,438	10/21/80	Fujino et al.	514	15	
JRL	11.	4,253,998	03/03/81	Sarantakis	525	54.11	
JRL	12.	4,277,394	07/07/81	Fujino et al.	530	330	
JRL	13.	4,338,306	07/06/82	Kitao et al.	514	4	
JRL	14.	4,348,387	09/07/82	Brownlee et al.	514	4	
JRL	15.	4,410,547	10/18/83	Ueno et al.	514	557	
JRL	16.	4,469,681	09/04/84	Brownlee et al.	514	4	
JRL	17.	4,472,382	09/18/84	Labrie et al.	514	15	
JRL	18.	4,554,101	11/19/85	Hopp	514	17	
JRL	19.	4,579,730	04/01/86	Kidron et al.	514	3	
JRL	20.	4,585,754	04/29/86	Meisner et al.	514	8	
JRL	21.	4,622,392	11/11/86	Hong et al.	536	26.22	
JRL	22.	4,684,524	08/04/87	Eckenhoff et al.	424	469	
JRL	23.	4,698,264	10/06/87	Steinke	428	402.2	
JRL	24.	4,717,566	01/05/88	Eckenhoff et al.	424	438	
JRL	25.	4,744,976	05/17/88	Snipes et al.	424	408	

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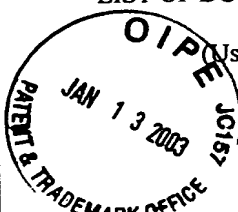
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FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary) 	Attorney Docket Number 9233-54	Serial No. 09/873,899
	Applicants: Ekwuribe et al.	
	Filing Date: 06/04/01	Group 1615

U. S. PATENT DOCUMENTS (CONT.)

JR	26.	4,772,471	09/20/88	Vanlerberghe et al.	424	450	
JR	27.	4,797,288	01/10/89	Sharma et al.	424	476	
JR	28.	4,839,341	06/13/89	Massey et al.	514	4	
JR	29.	4,840,799	06/20/89	Applegren et al.	424	493	
JR	30.	4,849,405	07/18/89	Ecanow	514	3	
JR	31.	4,917,888	04/17/90	Katre et al.	424	85.91	
JR	32.	4,935,246	06/19/90	Ahrens	424	490	
JR	33.	4,946,828	08/07/90	Markussen	514	3	
JR	34.	4,957,910	09/18/90	Sutton et al.	514	182	
JR	35.	4,963,367	10/16/90	Ecanow	424	485	
JR	36.	4,994,439	02/19/91	Longenecker et al.	514	3	
JR	37.	5,013,556	05/07/91	Woodle et al.	424	450	
JR	38.	5,055,300	10/08/91	Gupta	424	409	
JR	39.	5,055,304	10/08/91	Makino et al.	424	465	
JR	40.	5,089,261	02/18/92	Nitecki et al.	424	85.2	
JR	41.	5,093,198	03/03/92	Speaker et al.	428	402.21	
JR	42.	5,157,021	10/20/92	Balschmidt et al.	514	3	
JR	43.	5,162,430	11/10/92	Rhee et al.	525	54.1	
JR	44.	5,164,366	11/17/92	Balschmidt et al.	514	3	
JR	45.	5,202,415	04/13/93	Jonassen et al.	550	303	
JR	46.	5,206,219	04/27/93	Desai	514	3	
JR	47.	5,283,236	02/01/94	Chiou	514	2	
JR	48.	5,286,637	02/15/94	Veronese et al.	435	183	
JR	49.	5,304,473	04/19/94	Belagaje et al.	435	69.7	
JR	50.	5,312,808	05/17/94	Shorr et al.	514	6	
JR	51.	5,405,621	04/11/95	Sipos	424	490	
JR	52.	5,415,872	05/16/95	Sipos	424	490	
JR	53.	5,438,040	08/01/95	Ekwuribe	514	3	

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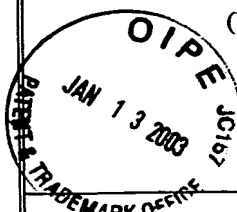
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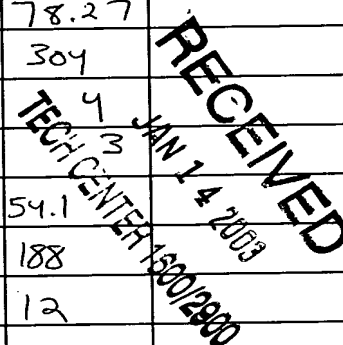
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U. S. PATENT DOCUMENTS (CONT.)

JRN	54.	5,444,041	08/22/95	Owen et al.	514	2	
JRN	55.	5,457,066	10/10/95	Frank et al.	435	68.1	
JRN	56.	5,461,031	10/24/95	De Felippis	514	4	
JRN	57.	5,468,478	11/21/95	Saifer et al.	424	78.27	
JRN	58.	5,504,188	04/02/96	Baker et al.	530	304	
JRN	59.	5,506,203	04/09/96	Backstrom et al.	514	4	
JRN	60.	5,518,998	05/21/96	Backstrom et al.	514	54.1	
JRN	61.	5,523,348	06/04/96	Rhee et al.	525	188	
JRN	62.	5,529,915	06/25/96	Phillips et al.	435	12	
JRN	63.	5,545,618	08/13/96	Buckley et al.	514	6.5	
JRN	64.	5,606,038	02/25/97	Regen	536	391.9	
JRN	65.	5,612,460	03/18/97	Zalipsky	530	303	
JRN	66.	5,631,347	05/20/97	Baker et al.	558	6	
JRN	67.	5,637,749	06/10/97	Greenwald	530	303	
JRN	68.	5,646,242	07/08/97	Baker et al.	514	6	
JRN	69.	5,650,388	07/22/97	Shorr et al.	514	3	
JRN	70.	5,658,878	08/19/97	Backstrom et al.	514	8	
JRN	71.	5,681,811	10/28/97	Ekwuribe	514	3	
JRN	72.	5,693,609	12/02/97	Baker et al.	536	5	
JRN	73.	5,693,769	12/02/97	Kahne et al.	530	305	
JRN	74.	5,700,904	12/23/97	Baker et al.	424	450	
JRN	75.	5,707,648	01/13/98	Yiv	424	85.7	
JRN	76.	5,738,846	04/14/98	Greenwald et al.	514	4	
JRN	77.	5,747,445	05/05/98	Backstrom et al.	530	304	
JRN	78.	5,747,642	05/05/98	De Felippis	514	3	
JRN	79.	5,750,497	05/12/98	Havelund et al.	424	436	
JRN	80.	5,766,620	06/16/98	Heiber et al.	514	3	
JRN	81.	5,824,638	10/20/98	Burnside et al.			



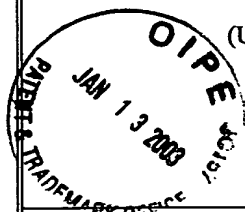
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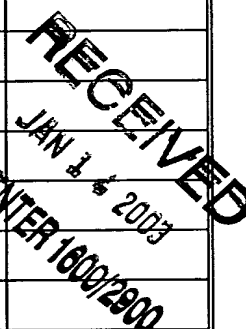
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U. S. PATENT DOCUMENTS (CONT.)

JR2	82.	5,830,853	11/03/98	Backstrom et al.	514	4	
JR2	83.	5,830,918	11/03/98	Sportsman et al.	514	648	
JR2	84.	5,849,860	12/15/98	Hakimi et al.	528	370	
JR2	85.	5,853,748	12/29/98	New	424	439	
JR2	86.	5,854,208	12/29/98	Jones et al.	514	3	
JR2	87.	5,856,451	01/05/99	Olsen et al.	530	402	
JR2	88.	5,866,538	02/02/99	Norup et al.	514	3	
JR2	89.	5,898,028	04/27/99	Jensen et al.	514	4	
JR2	90.	5,902,588	05/11/99	Greenwald et al.	424	278.1	
JR2	91.	5,905,140	05/18/99	Hansen	530	303	
JR2	92.	5,907,030	05/25/99	Shen et al.	530	331	
JR2	93.	5,922,675	07/13/99	Baker et al.	514	4	
JR2	94.	5,942,248	08/24/99	Barnwell	424	457	
JR2	95.	5,948,751	09/07/99	Kimer et al.	514	4	
JR2	96.	5,952,008	09/14/99	Backstrom et al.	424	499	
JR2	97.	5,952,297	09/14/99	De Felippis et al.	514	3	
JR2	98.	5,962,267	10/05/99	Shin et al.	435	69.4	
JR2	99.	5,968,549	10/19/99	New et al.	424	450	
JR2	100.	5,969,040	10/19/99	Hallahan et al.	525	54.1	
JR2	101.	5,981,709	11/09/99	Greenwald et al.	530	351	
JR2	102.	5,985,263	11/16/99	Lee et al.	424	85.2	
JR2	103.	6,004,574	12/21/99	Backstrom et al.	424	434	
JR2	104.	6,025,325	02/15/00	Campfield et al.	514	2	
JR2	105.	6,034,054	03/07/00	De Felippis et al.	514	34	
JR2	106.	6,043,214	03/28/00	Jensen et al.	514	3	
JR2	107.	6,051,551	04/18/00	Hughes et al.	514	3	
JR2	108.	6,063,761	05/16/00	Jones et al.	514	3	
JR2	109.	6,093,391	07/25/00	Kabanov et al.	424	85.1	


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U. S. PATENT DOCUMENTS (CONT.)

JR	110.	6,113,906	09/05/00	Greenwald et al.	424	199.1	
JR	111.	6,165,976	12/26/00	Backstrom et al.	514	3	
JR	112.	6,177,087	01/23/01	Greenwald et al.	424	278.1	
JR	113.	6,191,105	02/20/01	Ekwuribe et al.	514	3	
JR	114.	6,200,602	03/13/01	Watts et al.	424	463	
JR	115.	6,211,144	04/03/01	Havelund	514	4	
JR	116.	6,248,363	06/19/01	Patel et al.	424	497	
JR	117.	6,251,856	06/26/01	Markussen et al.	514	3	
JR	118.	6,258,377	07/10/01	New et al.	424	450	
JR	119.	6,268,335	07/31/01	Brader	514	3	
JR	120.	6,306,440	10/23/01	Backstrom et al.	424	499	
JR	121.	6,309,633	10/30/01	Ekwuribe et al.	424	85.1	
JR	122.	6,310,038	10/30/01	Havelund	514	4	
JR	123.	6,335,316	01/01/02	Hughes et al.	514	3	

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		Document Number	Date	Country	Class	Subclass	Translation Yes No
JR	124.	GB 1 492 997	11/23/77	Great Britain	—	—	Yes
JR	125.	EP 0 031 567	07/08/81	EPO	—	—	Yes
JR	126.	JP 1 254 699	10/11/89	Japan	—	—	No
JR	127.	WO 93/01802	02/04/93	PCT	—	—	Yes - abstract
JR	128.	WO 95/09831	04/13/95	PCT	—	—	Yes
JR	129.	WO 95/30641	11/16/95	PCT	—	—	Yes
JR	130.	EP 0 597 007	10/16/96	EPO	—	—	Yes
JR	131.	WO 98/07745	02/26/98	PCT	—	—	Yes

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JR	132.	Abuchowski, A. and F. F. Davis, "Soluble Polymer-Enzyme Adducts," pp. 368-383, Enzymes as Drugs, J. S. Holcenberg, John Wiley, 1981.					
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LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary)		JAN 14 2003 TECH. CENTER 1600/2900	
		Applicants: Ekwuribe et al.	
		Filing Date: 06/04/01	Group 1615
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) (CONT.)			
JR	133.	Akiyama, M. et al., "The Synthesis of New Derivatives of 1-.beta.-D-Arabinofuranosylcytosine," Chem. Pharm. Bull., 1978, 26(3): p. 981-984.	
JR	134.	Aoshima, M. et al., "N.sup.4 -Behenoyl-1-.beta.-D-Arabinofuranosylcytosine as a Potential New Antitumor Agent," Cancer Research, 1977, 37: pp. 2481-2486.	
JR	135.	Baker, D. C. et al., "Prodrugs of 9-.beta.-D-Arabinofuranosyladenine. 1. Synthesis and Evaluation of Some 5'-(O-Acyl) Derivatives," J. Med. Chem., 1978, 21(12): pp. 1218-1221.	
JR	136.	Banting et al., "Pancreatic Extracts in the Treatment of Diabetes Mellitus: Preliminary Report," Can. Med. Assoc. J., 145(10): 1281-1286 (1991).	
JR	137.	Baudys et al., "Stabilization and Intestinal Absorption of Human Calcitonin," J. Contr. Rel., 39: 145-51 (1996).	
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JR	140.	Brange, J., "Galenics of Insulin: The Physico-Chemical and Pharmaceutical Aspects of Insulin and Insulin Preparations," Novo Research Institute, Denmark, 18-100 (1987).	
JR	141.	Brange, J. et al, "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations," Pharm. Res., 1992, 9 (6): 715-726.	
JR	142.	Brange, J. et al, "Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation Products During Storage of Pharmaceutical Preparations," Pharm. Res., 1992, 9 (6) 727-734.	
JR	143.	Chien, Y. W., Novel Drug Delivery Systems, pp. 678-679, Marcell Deffer, Inc., New York, N.Y., 1992.	
JR	144.	Conradi, R.A., et al., "The Influence of Peptide Structure on Transport Across Caco-2 Cells," Pharm. Res., 1991, 8(12): 1453-1459.	
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JR	150.	Hashimoto et al., "Synthesis of Palmitoyl Derivatives of Insulin and Their Biological Activities," Pharmaceutical Research, 6(2): 171-176 (1989).	
JR	151.	Hostetler, K. Y. et al., "Synthesis and Antiretroviral Activity of Phospholipid Analogs of Azidothymidine and Other Antiviral Nucleosides," The Journal of Biological Chemistry, 1990, 265(11): pp. 6112-6117.	
JR	152.	Hong, C. I. et al., "Nucleoside Conjugates. 7. Synthesis and Antitumor Activity of 1-.beta.-D-Arabinofuranosylcytosine Conjugates of Ether Lipids," J. Med. Chem., 1986, 29: pp. 2038-2044.	
JR	153.	Igarashi, R. et al, "Biologically Active Peptides Conjugated with Lecithin for DDS" Proceed. Intern. Symp. Cont. Rel. Bioactiv. Mater. 1990, 17 367-368.	

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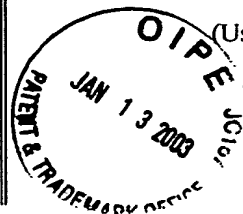
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) (CONT.)

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155.	Kemmler et al., "Studies on the Conversion of Proinsulin to Insulin: I. Conversion in Vitro with Trypsin and Carboxypeptidase B," The Journal of Biological Chemistry, 246(22) 6786-6791 (November 25, 1971).
156.	King et al.; "Preparation of Protein Conjugates with Alkoxypolyethylene Glycols" Int. J. Peptide Protein Res. 16 147-155 (1980).
157.	M. Maislos et al, "The Source of the Circulating Aggregate of Insulin in Type I Diabetic Patients is Therapeutic Insulin" J. Clin. Invest., 1986, 77: 717-723.
158.	Nucci, et al. "The Therapeutic Value of Poly(ethylen Glycol)--Modified Proteins" Ac. Drug. Del. Rev. 6: 133-151 1991.
159.	Oka, K. et al, "Enhanced Intestinal Absorption of a Hydrophobic Polymer-conjugated Protein Drug, Smanes, in an Oily Formulation" Pharm. Res., 1990, 7 (8): 852-855.
160.	Patel et al. "Oral Administration of Insulin By Encapsulation Within Liposomes" FEBS Lett. 62(1) 60-63 1976.
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162.	Ratner, R. E. et al, "Persistent Cutaneous Insulin Allergy Resulting from High-Molecular Weight Insulin Aggregates," Diabetes, 1990, 39: 728-733.
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Jeffrey E. Russell

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